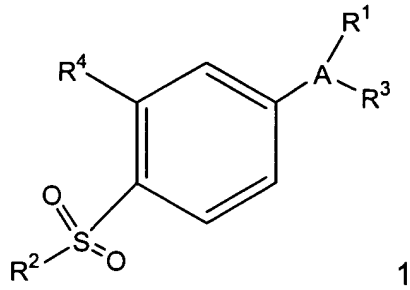
IN THE CLAIMS

1. (Presently Amended) A method for treating, ~~preventing or reducing the risk of developing~~ a neoplasia disorder in a mammal in need thereof, comprising administering to the mammal in a combination therapy an amount of a DNA topoisomerase I inhibiting agent and an amount of a selective COX-2 inhibiting agent wherein the amount of the DNA topoisomerase I inhibiting agent and the selective COX-2 inhibiting agent together make a neoplasia disorder effective amount.

2. (Original) The method of claim 1 wherein the DNA topoisomerase I inhibiting agent is selected from the group consisting of irinotecan; irinotecan hydrochloride; camptothecin; 9-aminocamptothecin; 9-nitrocamptothecin; 9-chloro-10-hydroxy camptothecin; topotecan; topotecan hydrochloride; lurtotecan; lurtotecan dihydrochloride; lurtotecan (liposomal); homosilatecans; 6,8-dibromo-2-methyl-3-[2-(D-xylopyranosylamino)phenyl]-4(3H)-quinazolinone; 2-cyano-3-(3,4-dihydroxyphenyl)-N-(phenylmethyl)-(2E)-2-propenamide; 2-cyano-3-(3,4-dihydroxyphenyl)-N-(3-hydroxyphenylpropyl)-(E)-2-propenamide; 5H-indolo[2,3-a]pyrrolo[3,4-c]carbazole-5,7(6H)-dione, 12-.beta.-D-glucopyranosyl-12,13-dihydro-2,10-dihydroxy-6-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino]; 4-acridinecarboxamide, N-[2-(dimethylamino)ethyl], dihydrochloride; and 4-acridinecarboxamide, N-[2-(dimethylamino)ethyl].

3. (Original) The method of claim 2 wherein the DNA topoisomerase I inhibiting agent is selected from the group consisting of irinotecan, irinotecan hydrochloride, camptothecin, 9-aminocamptothecin, 9-nitrocamptothecin, 9-chloro-10-hydroxy camptothecin, topotecan, topotecan hydrochloride, lurtotecan, lurtotecan dihydrochloride, lurtotecan (liposomal), and homosilatecans.

4. (Original) The method of claim 1 wherein the selective COX-2 inhibiting agent is selected from compounds of Formula 1:



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or a pharmaceutically-acceptable salt or prodrug thereof,

wherein

A is a 5- or 6-member ring substituent selected from the group consisting of heterocyclyl and carbocyclyl, wherein A is optionally substituted with one or more radicals selected from the group consisting of hydroxy, alkyl, halo, oxo, and alkoxy;

R^1 is selected from the group consisting of cyclohexyl, pyridinyl, and phenyl, wherein R^1 is optionally substituted with one or more radicals selected from the group consisting of alkyl, haloalkyl, cyano, carboxyl, alkoxycarbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, phenylamino, nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy, and alkylthio;

R^2 is selected from the group consisting of alkyl and amino;

R^3 is selected from the group consisting of halo, alkyl, alkenyl, alkynyl, aryl, heteroaryl, oxo, cyano, carboxyl, cyanoalkyl, heterocyclyloxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkyl, phenyl, haloalkyl, heterocyclo, cycloalkenyl, phenylalkyl, heterocycloalkyl, alkylthioalkyl, hydroxyalkyl, alkoxycarbonyl, phenylcarbonyl, phenylalkylcarbonyl, phenylalkenyl, alkoxyalkyl, phenylthioalkyl, phenyloxyalkyl, alkoxyphenylalkoxyalkyl, alkoxycarbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-phenylaminocarbonyl, N-alkyl-N-phenylaminocarbonyl, alkylaminocarbonylalkyl, carboxyalkyl, alkylamino, N-arylamino, N-arylkylamino, N-alkyl-N-arylkylamino, N-alkyl-N-arylamino, aminoalkyl, alkylaminoalkyl, N-phenylaminoalkyl, N-phenylalkylaminoalkyl, N-alkyl-N-phenylalkylaminoalkyl, N-alkyl-N-phenylaminoalkyl, phenyloxy, phenylalkoxy, phenylthio, phenylalkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-phenylaminosulfonyl, phenylsulfonyl, and N-alkyl-N-phenylaminosulfonyl; and

R^4 is selected from the group consisting of hydrido and halo.

5. (Original) The method of claim 4 wherein A is selected from the group consisting of thienyl, oxazolyl, furyl, furanone, pyrrolyl, thiazolyl, imidazolyl, benzofuryl, indenyl, benzithienyl, isoxazolyl, pyrazolyl, cyclopentenyl, cyclopentadienyl, benzindazolyl, cyclopentenone, benzopyranopyrazolyl, phenyl, and pyridyl.

6. (Withdrawn) The method of claim 5 wherein A is substituted with one or more radicals selected from the group consisting of alkyl, halo, oxo, hydroxy and alkoxy.

7. (Original) The method of claim 4 wherein R^1 is selected from the group consisting of cyclohexyl, pyridinyl, and phenyl, wherein cyclohexyl, pyridinyl, and phenyl are optionally substituted with one or more radicals selected from the group consisting of alkyl, haloalkyl, cyano, carboxyl, alkoxycarbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, phenylamino, nitro, alkoxyalkyl, alkylsulfinyl, alkoxy, halo, alkoxy, and alkylthio.

8. (Original) The method of claim 7 wherein R^1 is selected from the group consisting of pyridyl, cyclohexyl, and phenyl, wherein R^1 is optionally substituted with one or more radicals selected from the group consisting of alkyl, halo, and alkoxy.

9. (Original) The method of claim 4 wherein R^2 is selected from the group consisting of methyl and amino.

10. (Original) The method of claim 4 wherein R^3 is selected from the group consisting of halo, alkyl, alkenyl, alkynyl, aryl, heteroaryl, oxo, hydroxyl, cyano, carboxyl, cyanoalkyl, heterocyclyloxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkyl, phenyl, haloalkyl, heterocyclo, cycloalkenyl, phenylalkyl, heterocyclylalkyl, alkylthioalkyl, hydroxyalkyl, alkoxycarbonyl, phenylcarbonyl, phenylalkylcarbonyl, phenylalkenyl, alkoxyalkyl, phenylthioalkyl, phenyloxyalkyl,

alkoxyphenylalkoxyalkyl, alkoxycarbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-phenylaminocarbonyl, N-alkyl-N-phenylaminocarbonyl, alkylaminocarbonyl-alkyl, carboxy-alkyl, alkylamino, N-arylamino, N-arylkylamino, N-alkyl-N-arylkylamino, N-alkyl-N-arylamino, amino-alkyl, alkylaminoalkyl, N-phenylamino-alkyl, N-phenyl-alkylaminoalkyl, N-alkyl-N-phenyl-alkylamino-alkyl, N-alkyl-N-phenylaminoalkyl, phenyloxy, phenylalkoxy, phenylthio, phenylalkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-phenylaminosulfonyl, phenylsulfonyl, and N-alkyl-N-phenylaminosulfonyl.

11. (Original) The method of claim 10 wherein R^3 is a selected from the group consisting of halo, alkyl, cyano, carboxyl, alkyloxy, phenyl, haloalkyl, and hydroxyalkyl.

12. (Original) The method of claim 4 wherein the selective COX-2 inhibiting agent is selected from the group consisting of
rofecoxib,
celecoxib,
valdecoxib,
deracoxib,
etoricoxib,
4-(4-cyclohexyl-2-methyloxazol-5-yl)-2-fluorobenzenesulfonamide,
5-chloro-3-(4-(methylsulfonyl)phenyl)-2-(methyl-5-pyridinyl)pyridine,
2-(3,5-difluorophenyl)-3-4-(methylsulfonyl)phenyl)-2-cyclopenten-1-one,
N-[[4-(5-methyl-3-phenylisoxazol-4yl]phenyl]sulfonyl]propanamide,
4-[5-(4-chorophenyl)-3-(trifluoromethyl)-1H-pyrazole-1-yl]benzenesulfonamide,
3-(3,4-difluorophenoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-2(5H)-furanone,
N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,
3-(4-chlorophenyl)-4-[4-(methylsulfonyl)phenyl]-2(3H)-oxazolone,
4-[3-(4-fluorophenyl)-2,3-dihydro-2-oxo-4-oxazolyl]benzenesulfonamide,

3-[4-(methylsulfonyl)phenyl]-2-phenyl-2-cyclopenten-1-one,

4-(2-methyl-4-phenyl-5-oxazolyl)benzenesulfonamide,

3-(4-fluorophenyl)-4-[4-(methylsulfonyl)phenyl]-2(3H)-oxazolone,

5-(4-fluorophenyl)-1-[4-(methylsulfonyl)phenyl]-3-(trifluoromethyl)-1H-pyrazole,

4-[5-phenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide,

4-[1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]benzenesulfonamide,

4-[5-(4-fluorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide,

N-[2-(cyclohexyloxy)-4-nitrophenyl]methanesulfonamide,

N-[6-(2,4-difluorophenoxy)-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,

3-(4-chlorophenoxy)-4-[(methylsulfonyl)amino]benzenesulfonamide,

3-(4-fluorophenoxy)-4-[(methylsulfonyl)amino]benzenesulfonamide,

3-[(1-methyl-1H-imidazol-2-yl)thio]-4 [(methylsulfonyl) amino]benzenesulfonamide,

5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-3-phenoxy-2(5H)-furanone,

N-[6-[(4-ethyl-2-thiazolyl)thio]-1,3-dihydro-1-oxo-5-isobenzofuranyl]methanesulfonamide,

3-[(2,4-dichlorophenyl)thio]-4-[(methylsulfonyl)amino] benzenesulfonamide,

1-fluoro-4-[2-[4-(methylsulfonyl)phenyl]cyclopenten-1-yl]benzene,

4-[5-(4-chlorophenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide,

3-[1-[4-(methylsulfonyl)phenyl]-4-(trifluoromethyl)-1H-imidazol-2-yl]pyridine,

4-[2-(3-pyridinyll)-4-(trifluoromethyl)-1H-imidazol-1-yl]benzenesulfonamide,

4-[5-(hydroxymethyl)-3-phenylisoxazol-4-yl]benzenesulfonamide,

4-[3-(4-chlorophenyl)-2,3-dihydro-2-oxo-4-oxazolyl]benzenesulfonamide,

4-[5-(difluoromethyl)-3-phenylisoxazol-4-yl]benzenesulfonamide,

[1,1':2',1"-terphenyl]-4-sulfonamide,

4-(methylsulfonyl)-1,1',2],1"-terphenyl,

4-(2-phenyl-3-pyridinyl)benzenesulfonamide,

N-(2,3-dihydro-1,1-dioxido-6-phenoxy-1,2-benzisothiazol-5-yl)methanesulfonamide,

N-[3-(formylamino)-4-oxo-6-phenoxy-4H-1-benzopyran-7-yl]methanesulfonamide,

6-[[5-(4-chlorobenzoyl)-1,4—dimethyl-1H-pyrrol-2-yl]methyl]-3(2H)-pyridazinone,

and

N-(4-nitro-2-phenoxyphenyl)methanesulfonamide.

13. (Withdrawn) The method of claim 12 wherein the selective COX-2 inhibiting agent is rofecoxib.

14. (Original) The method of claim 12 wherein the selective COX-2 inhibiting agent is celecoxib.

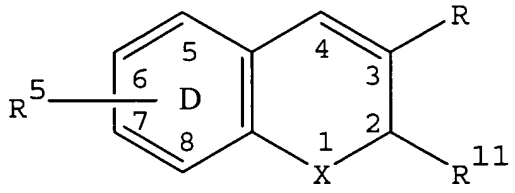
15. (Withdrawn) The method of claim 12 wherein the selective COX-2 inhibiting agent is valdecoxib.

16. (Withdrawn) The method of claim 12 wherein the selective COX-2 inhibiting agent is deracoxib.

17. (Withdrawn) The method of claim 12 wherein the selective COX-2 inhibiting agent is 4-(4-cyclohexyl-2-methyloxazol-5-yl)-2-fluorobenzenesulfonamide.

18. (Withdrawn) The method of claim 12 wherein the selective COX-2 inhibiting agent is etoricoxib.

19. (Withdrawn) The method of claim 1 wherein the selective COX-2 inhibiting agent is selected from compounds of Formula 2:



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or an isomer or pharmaceutically-acceptable salt or prodrug thereof,

wherein

X is selected from the group consisting of O, S and NR^a;

R^a is alkyl;

R is selected from the group consisting of carboxyl, alkyl, aralkyl, aminocarbonyl, alkylsulfonylaminocarbonyl and alkoxycarbonyl;

R^{11} is selected from the group consisting of haloalkyl, alkyl, aralkyl, cycloalkyl and aryl, wherein aryl is optionally substituted with one or more radicals selected from the group consisting of alkylthio, nitro and alkylsulfonyl; and

R^5 is one or more radicals independently selected from the group consisting of hydrido, halo, alkyl, aralkyl, alkoxy, aryloxy, heteroaryloxy, aralkyloxy, heteroaralkyloxy, haloalkyl, haloalkoxy, alkylamino, arylamino, aralkylamino, heteroarylamino, heteroarylalkylamino, nitro, amino, aminosulfonyl, alkylaminosulfonyl, arylaminosulfonyl, heteroarylaminosulfonyl, aralkylaminosulfonyl, heteroaralkylaminosulfonyl, heterocyclosulfonyl, alkylsulfonyl, optionally substituted aryl, optionally substituted heteroaryl, aralkylcarbonyl, heteroarylcarbonyl, arylcarbonyl, aminocarbonyl, and alkylcarbonyl, wherein R^5 together with ring D optionally forms a naphthyl radical.

20. (Withdrawn) The method of claim 19 wherein X is selected from the group consisting of O and S.

21. (Withdrawn) The method of claim 19 wherein R is selected from the group consisting of carboxyl, lower alkyl, lower aralkyl and lower alkoxycarbonyl.

22. (Withdrawn) The method of claim 21 wherein R is carboxyl.

23. (Withdrawn) The method of claim 19 wherein R^{11} is selected from the group consisting of lower haloalkyl, lower cycloalkyl and phenyl.

24. (Withdrawn) The method of claim 23 wherein R^{11} is lower haloalkyl.

25. (Withdrawn) The method of claim 24 wherein R^{11} is selected from the group consisting of fluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, difluoromethyl, and trifluoromethyl.

26. (Withdrawn) The method of claim 25 wherein R^{11} is selected from the group consisting of trifluoromethyl and pentafluorethyl.

27. (Withdrawn) The method of claim 19 wherein R^5 is one or more radicals independently selected from the group consisting of hydrido, halo, lower alkyl, lower alkoxy, lower haloalkyl, lower haloalkoxy, lower alkylamino, nitro, amino, aminosulfonyl, lower alkylaminosulfonyl, 5- or 6- membered heteroarylalkylaminosulfonyl, lower aralkylaminosulfonyl, 5- or 6- membered nitrogen containing heterocyclosulfonyl, lower alkylsulfonyl, optionally substituted phenyl, lower aralkylcarbonyl, and lower alkylcarbonyl.

28. (Withdrawn) The method of claim 27 wherein R^5 is one or more radicals independently selected from the group consisting of hydrido, chloro, fluoro, bromo, iodo, methyl, ethyl, isopropyl, *tert*-butyl, butyl, isobutyl, pentyl, hexyl, methoxy, ethoxy, isopropyloxy, tertbutyloxy, trifluoromethyl, difluoromethyl, trifluoromethoxy, amino, N,N-dimethylamino, N,N-diethylamino, N-phenylmethylaminosulfonyl, N-phenylethylaminosulfonyl, N-(2-furylmethyl)aminosulfonyl, nitro, N,N-dimethylaminosulfonyl, aminosulfonyl, N-methylaminosulfonyl, N-ethylsulfonyl, 2,2-dimethylethylaminosulfonyl, N,N-dimethylaminosulfonyl, N-(2-methylpropyl)aminosulfonyl, N-morpholinosulfonyl, methylsulfonyl, benzylcarbonyl, 2,2-dimethylpropylcarbonyl, phenylacetyl and phenyl.

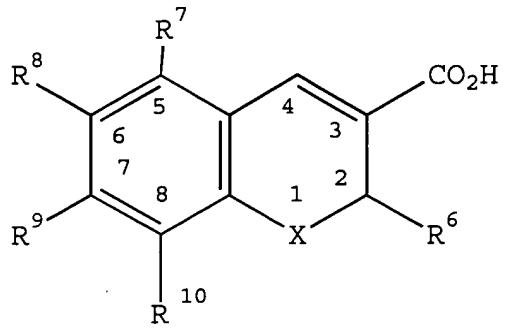
29. (Withdrawn) The method of claim 28 wherein R^5 is one or more radicals independently selected from the group consisting of hydrido, chloro, fluoro, bromo, iodo, methyl, ethyl, isopropyl, *tert*-butyl, methoxy, trifluoromethyl, trifluoromethoxy, N-phenylmethylaminosulfonyl, N-phenylethylaminosulfonyl, N-(2-furylmethyl)aminosulfonyl, N,N-dimethylaminosulfonyl, N-methylaminosulfonyl, N-(2,2-dimethylethyl)aminosulfonyl, dimethylaminosulfonyl, 2-methylpropylaminosulfonyl, N-morpholinosulfonyl, methylsulfonyl, benzylcarbonyl, and phenyl.

30. (Withdrawn) The method of claim 19 wherein the selective COX-2 inhibiting agent is selected from the group consisting of
6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
2-trifluoromethyl-3H-naphthopyran-3-carboxylic acid,
7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-bromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
5,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
7,8-dimethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,8-bis(dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
7-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-8-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,8-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

2-trifluoromethyl-3H-naptho[2,1-b]pyran-3-carboxylic acid,
6-chloro-8-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-6-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-bromo-8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-bromo-6-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-bromo-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-bromo-5-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-8-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-bromo-8-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[[(phenylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[(dimethylamino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[(methylamino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[(4-morpholino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[(1,1-dimethylethyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[(2-methylpropyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-methylsulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-6-[[(phenylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-phenylacetyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,8-dibromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-5,6-dimethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,8-dichloro-(*S*)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-benzylsulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[[N-(2-furylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[[N-(2-phenylethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-iodo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

7-(1,1-dimethylethyl)-2-pentafluoroethyl-2H-1-benzopyran-3-carboxylic acid, and 6-chloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid.

31. (Withdrawn) The method of claim 1 wherein the selective COX-2 inhibiting agent is selected from compounds of Formula 3:



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or an isomer or pharmaceutically-acceptable salt or prodrug thereof, wherein

X is selected from the group consisting of O and S;

R^6 is lower haloalkyl;

R^7 is selected from the group consisting of hydrido and halo;

R^8 is selected from the group consisting of hydrido, halo, lower alkyl, lower haloalkoxy, lower alkoxy, lower aralkylcarbonyl, lower dialkylaminosulfonyl, lower alkylaminosulfonyl, lower aralkylaminosulfonyl, lower heteroaralkylaminosulfonyl, and 5- or 6- membered nitrogen containing heterocyclosulfonyl;

R^9 is selected from the group consisting of hydrido, lower alkyl, halo, lower alkoxy, and aryl; and

R^{10} is selected from the group consisting of hydrido, halo, lower alkyl, lower alkoxy, and aryl.

32. (Withdrawn) The method of claim 31 wherein R^6 is selected from the group consisting of trifluoromethyl and pentafluoroethyl.

33. (Withdrawn) The method of claim 31 wherein R^7 is selected from the group consisting of hydrido, chloro, and fluoro.

34. (Withdrawn) The method of claim 31 wherein R^8 is selected from the group consisting of hydrido, chloro, bromo, fluoro, iodo, methyl, tert-butyl, trifluoromethoxy, methoxy, benzylcarbonyl, dimethylaminosulfonyl, isopropylaminosulfonyl, methylaminosulfonyl, benzylaminosulfonyl, phenylethylaminosulfonyl, methylpropylaminosulfonyl, methylsulfonyl, and morpholinosulfonyl.

35. (Withdrawn) The method of claim 31 wherein R^9 is selected from the group consisting of hydrido, methyl, ethyl, isopropyl, tert-butyl, chloro, methoxy, diethylamino, and phenyl.

36. (Withdrawn) The method of claim 31 wherein R^{10} is selected from the group consisting of hydrido, chloro, bromo, fluoro, methyl, ethyl, tert-butyl, methoxy, and phenyl.

37. (Withdrawn) The method of claim 31 wherein the selective COX-2 inhibiting agent is selected from the group consisting of
6-Chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-Chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-Chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-Chloro-7-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-Trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-Trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-Formyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-(Difluoromethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,8-Dichloro-7-methyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,

6,8-Dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6,8-Dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-Chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
(S)-6-chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
6,8-Dichloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
7-(1,1-Dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,7-Dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
5,6-Dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
2,6-Bis(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
5,6,7-Trichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,7,8-Trichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-Iodo-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
6-Bromo-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
6-Chloro-7-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid, and
6,8-Dichloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid.

38. (Withdrawn) The method of claim 37 wherein the selective COX-2 inhibiting agent is selected from the group consisting of
6-Chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-Chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-Chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-Chloro-7-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-Trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-Trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-Formyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-(Difluoromethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,8-Dichloro-7-methyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,8-Dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6,8-Dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-Chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,

(S)-6-chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid, and
6,8-Dichloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid.

39. (Withdrawn) The method of claim 1 wherein the selective COX-2 inhibiting agent is selected from compounds that correspond in structure, and pharmaceutically acceptable salts thereof, of the group consisting of:
N-(2,3-dihydro-1,1-dioxido-6-phenoxy-1,2-benzisothiazol-5-yl)methanesulfonamide,
6-[[5-(4-chlorobenzoyl)-1,4—dimethyl-1H-pyrrol-2-yl]methyl]-3(2H)-pyridazinone,
N-(4-nitro-2-phenoxyphenyl)methanesulfonamide,
3-(3,4-difluorophenoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-2(5H)-furanone,
N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,
N-[2-(cyclohexyloxy)-4-nitrophenyl]methanesulfonamide,
N-[6-(2,4-difluorophenoxy)-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,
3-(4-chlorophenoxy)-4-[(methylsulfonyl)amino]benzenesulfonamide,
3-(4-fluorophenoxy)-4-[(methylsulfonyl)amino]benzenesulfonamide,
3-[(1-methyl-1H-imidazol-2-yl)thio]-4 [(methylsulfonyl) amino]benzenesulfonamide,
5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-3-phenoxy-2(5H)-furanone,
N-[6-[(4-ethyl-2-thiazolyl)thio]-1,3-dihydro-1-oxo-5-isobenzofuranyl]methanesulfonamide,
3-[(2,4-dichlorophenyl)thio]-4-[(methylsulfonyl)amino]benzenesulfonamide,
N-(2,3-dihydro-1,1-dioxido-6-phenoxy-1,2-benzisothiazol-5-yl)methanesulfonamide, and
N-[3-(formylamino)-4-oxo-6-phenoxy-4H-1-benzopyran-7-yl]methanesulfonamide.

40. (Original) The method of claim 1 wherein the neoplasia disorder is selected from the group consisting of a lung, a breast, a skin, a stomach, an intestine, an

esophagus, a bladder, a head, a neck, a brain, a cervical, and an ovary neoplasia disorder.

41. (Original) The method of claim 1 wherein the neoplasia disorder is selected from the group consisting of acral lentiginous melanoma, an actinic keratosis, adenocarcinoma, adenoid cycstic carcinoma, an adenoma, adenosarcoma, adenosquamous carcinoma, an astrocytic tumor, bartholin gland carcinoma, basal cell carcinoma, a bronchial gland carcinoma, capillary carcinoma, a carcinoid, carcinoma, carcinosarcoma, cavernous carcinoma, cholangiocarcinoma, chondosarcoma, choriod plexus papilloma, choriod plexus carcinoma, clear cell carcinoma, cystadenoma, endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, ependymal carcinoma, epitheloid carcinoma, Ewing's sarcoma, fibrolamellar, focal nodular hyperplasia, gastrinoma, a germ cell tumor, glioblastoma, glucagonoma, hemangiblastoma, hemangioendothelioma, a hemangioma, hepatic adenoma, hepatic adenomatosis, hepatocellular carcinoma, insulinoma, intaepithelial neoplasia, interepithelial squamous cell neoplasia, invasive squamous cell carcinoma, large cell carcinoma, leiomyosarcoma, a lentigo maligna melanoma, malignant melanoma, a malignant mesothelial tumor, medulloblastoma, medulloepithelioma, melanoma, meningeal, mesothelial, metastatic carcinoma, mucoepidermoid carcinoma, neuroblastoma, neuroepithelial adenocarcinoma nodular melanoma, oat cell carcinoma, oligodendroglial, osteosarcoma, pancreatic polypeptide, papillary serous adenocarcinoma, pineal cell, a pituitary tumor, plasmacytoma, pseudosarcoma, pulmonary blastoma, renal cell carcinoma, retinoblastoma, rhabdomyosarcoma, sarcoma, serous carcinoma, small cell carcinoma, a soft tissue carcinoma, somatostatin-secreting tumor, squamous carcinoma, squamous cell carcinoma, submesothelial, superficial spreading melanoma, undifferentiated carcinoma, uveal melanoma, verrucous carcinoma, vipoma, a well differentiated carcinoma, and Wilm's tumor.

42. (Original) The method of claim 1 wherein the selective COX-2 inhibiting agent and the DNA topoisomerase I inhibiting agent are formulated in a single composition.

43. (Original) The method of claim 1 wherein the selective COX-2 inhibiting agent and the DNA topoisomerase I inhibiting agent are provided as a separate component of a kit.

44. (Original) The method of claim 1 wherein the mammal is a human.

45. (Original) The method of claim 1 wherein the selective COX-2 inhibiting agent and the DNA topoisomerase I inhibiting agent are administered in a sequential manner.

46. (Original) The method of claim 1 wherein the selective COX-2 inhibiting agent and the DNA topoisomerase I inhibiting agent are administered in a substantially simultaneous manner.

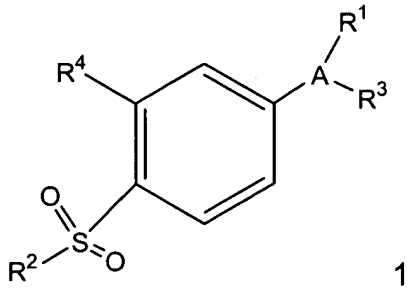
47. (Original) A pharmaceutical composition comprising a DNA topoisomerase I inhibiting agent and a COX-2 inhibiting agent wherein the DNA topoisomerase I inhibiting agent and the selective COX-2 inhibiting agent together make a neoplasia disorder effective amount.

48. (Original) The pharmaceutical composition of claim 47 wherein the DNA topoisomerase I inhibiting agent is selected from the group consisting of irinotecan; irinotecan hydrochloride; camptothecin; 9-aminocamptothecin; 9-nitrocamptothecin; 9-chloro-10-hydroxy camptothecin; topotecan; topotecan hydrochloride; lurtotecan; lurtotecan dihydrochloride; lurtotecan (liposomal); homosilatecans; 6,8-dibromo-2-methyl-3-[2-(D-xylopyranosylamino)phenyl]-4(3H)-quinazolinone; 2-cyano-3-(3,4-dihydroxyphenyl)-N-(phenylmethyl)-(2E)-2-propenamide; 2-cyano-3-(3,4-dihydroxyphenyl)-N-(3-hydroxyphenylpropyl)-(E)-2-propenamide; 5H-indolo[2,3-a]pyrrolo[3,4-c]carbazole-5,7(6H)-dione, 12-.beta.-

D-glucopyranosyl-12,13-dihydro-2,10-dihydroxy-6-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino]; 4-acridinecarboxamide, N-[2-(dimethylamino)ethyl], dihydrochloride; and 4-acridinecarboxamide, N-[2-(dimethylamino)ethyl].

49. (Original) The pharmaceutical composition of claim 48 wherein the DNA topoisomerase I inhibiting agent is selected from the group consisting of irinotecan, irinotecan hydrochloride, camptothecin, 9-aminocamptothecin, 9-nitrocamptothecin, 9-chloro-10-hydroxy camptothecin, topotecan, topotecan hydrochloride, lurtotecan, lurtotecan dihydrochloride, lurtotecan (liposomal), and homosilatecans.

50. (Original) The pharmaceutical composition of claim 47 wherein the selective COX-2 inhibiting agent is selected from compounds of Formula 1:



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or a pharmaceutically-acceptable salt or prodrug thereof,
wherein

A is a 5- or 6-member ring substituent selected from the group consisting of heterocyclyl and carbocyclyl, wherein A is optionally substituted with one or more radicals selected from the group consisting of hydroxy, alkyl, halo, oxo, and alkoxy;

R^1 is selected from the group consisting of cyclohexyl, pyridinyl, and phenyl, wherein R^1 is optionally substituted with one or more radicals selected from the group consisting of alkyl, haloalkyl, cyano, carboxyl, alkoxycarbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, phenylamino, nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy, and alkylthio;

R^2 is selected from the group consisting of alkyl and amino;

R^3 is selected from the group consisting of halo, alkyl, alkenyl, alkynyl, aryl, heteroaryl, oxo, cyano, carboxyl, cyanoalkyl, heterocyclyloxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkyl, phenyl, haloalkyl, heterocyclo, cycloalkenyl, phenylalkyl, heterocycloalkyl, alkylthioalkyl, hydroxyalkyl, alkoxycarbonyl, phenylcarbonyl, phenylalkylcarbonyl, phenylalkenyl, alkoxyalkyl, phenylthioalkyl, phenyloxyalkyl, alkoxyphenylalkoxyalkyl, alkoxycarbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-phenylaminocarbonyl, N-alkyl-N-phenylaminocarbonyl, alkylaminocarbonylalkyl, carboxyalkyl, alkylamino, N-arylamino, N-arylkylamino, N-alkyl-N-arylkylamino, N-alkyl-N-arylamino, aminoalkyl, alkylaminoalkyl, N-phenylaminoalkyl, N-phenylalkylaminoalkyl, N-alkyl-N-phenylalkylaminoalkyl, N-alkyl-N-phenylaminoalkyl, phenyloxy, phenylalkoxy, phenylthio, phenylalkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-phenylaminosulfonyl, phenylsulfonyl, and N-alkyl-N-phenylaminosulfonyl; and

R^4 is selected from the group consisting of hydrido and halo.

51. (Original) The pharmaceutical composition of claim wherein A is selected from the group consisting of thienyl, oxazolyl, furyl, furanone, pyrrolyl, thiazolyl, imidazolyl, benzofuryl, indenyl, benzithienyl, isoxazolyl, pyrazolyl, cyclopentenyl, cyclopentadienyl, benzindazolyl, cyclopentenone, benzopyranopyrazolyl, phenyl, and pyridyl.

52. (Withdrawn) The pharmaceutical composition of claim 51 wherein A is substituted with one or more radicals selected from the group consisting of alkyl, halo, oxo, hydroxy and alkoxy.

53. (Original) The pharmaceutical composition of claim 50 wherein R^1 is selected from the group consisting of cyclohexyl, pyridinyl, and phenyl, wherein cyclohexyl, pyridinyl, and phenyl are optionally substituted with one or more radicals selected from the group consisting of alkyl, haloalkyl, cyano, carboxyl, alkoxycarbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, phenylamino, nitro, alkoxyalkyl, alkylsulfinyl, alkoxy, halo, alkoxy, and alkylthio.

54. (Original) The pharmaceutical composition of claim 53 wherein R^1 is selected from the group consisting of pyridyl, cyclohexyl, and phenyl, wherein R^1 is optionally substituted with one or more radicals selected from the group consisting of alkyl, halo, and alkoxy.

55. (Original) The pharmaceutical composition of claim 50 wherein R^2 is selected from the group consisting of methyl and amino.

56. (Original) The pharmaceutical composition of claim 50 wherein R^3 is selected from the group consisting of halo, alkyl, alkenyl, alkynyl, aryl, heteroaryl, oxo, hydroxyl, cyano, carboxyl, cyanoalkyl, heterocyclyloxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkyl, phenyl, haloalkyl, heterocyclo, cycloalkenyl, phenylalkyl, heterocyclylalkyl, alkylthioalkyl, hydroxyalkyl, alkoxycarbonyl, phenylcarbonyl, phenylalkylcarbonyl, phenylalkenyl, alkoxyalkyl, phenylthioalkyl, phenyloxyalkyl, alkoxyphenylalkoxyalkyl, alkoxycarbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-phenylaminocarbonyl, N-alkyl-N-phenylaminocarbonyl, alkylaminocarbonyl-alkyl, carboxy-alkyl, alkylamino, N-arylamino, N-arylkylamino, N-alkyl-N-arylkylamino, N-alkyl-N-arylamino, amino-alkyl, alkylaminoalkyl, N-phenylamino-alkyl, N-phenyl-alkylaminoalkyl, N-alkyl-N-phenyl-alkylamino-alkyl, N-alkyl-N-phenylaminoalkyl, phenyloxy, phenylalkoxy, phenylthio, phenylalkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-phenylaminosulfonyl, phenylsulfonyl, and N-alkyl-N-phenylaminosulfonyl.

57. (Original) The pharmaceutical composition of claim 56 wherein R^3 is a selected from the group consisting of halo, alkyl, cyano, carboxyl, alkyloxy, phenyl, haloalkyl, and hydroxyalkyl.

58. (Original) The pharmaceutical composition of claim 50 wherein the selective COX-2 inhibiting agent is selected from the group consisting of rofecoxib,

celecoxib,

valdecoxib,

deracoxib,

etoricoxib,

4-(4-cyclohexyl-2-methyloxazol-5-yl)-2-fluorobenzenesulfonamide,

5-chloro-3-(4-(methylsulfonyl)phenyl)-2-(methyl-5-pyridinyl)pyridine,

2-(3,5-difluorophenyl)-3-4-(methylsulfonyl)phenyl)-2-cyclopenten-1-one,

N-[[4-(5-methyl-3-phenylisoxazol-4yl]phenyl]sulfonyl]propanamide,

4-[5-(4-chorophenyl)-3-(trifluoromethyl)-1H-pyrazole-1-yl]benzenesulfonamide,

3-(3,4-difluorophenoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-2(5H)-furanone,

N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,

3-(4-chlorophenyl)-4-[4-(methylsulfonyl)phenyl]-2(3H)-oxazolone,

4-[3-(4-fluorophenyl)-2,3-dihydro-2-oxo-4-oxazolyl]benzenesulfonamide,

3-[4-(methylsulfonyl)phenyl]-2-phenyl-2-cyclopenten-1-one,

4-(2-methyl-4-phenyl-5-oxazolyl)benzenesulfonamide,

3-(4-fluorophenyl)-4-[4-(methylsulfonyl)phenyl]-2(3H)-oxazolone,

5-(4-fluorophenyl)-1-[4-(methylsulfonyl)phenyl]-3-(trifluoromethyl)-1H-pyrazole,

4-[5-phenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide,

4-[1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]benzenesulfonamide,

4-[5-(4-fluorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide,

N-[2-(cyclohexyloxy)-4-nitrophenyl]methanesulfonamide,

N-[6-(2,4-difluorophenoxy)-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,

3-(4-chlorophenoxy)-4-[(methylsulfonyl)amino]benzenesulfonamide,

3-(4-fluorophenoxy)-4-[(methylsulfonyl)amino]benzenesulfonamide,

3-[(1-methyl-1H-imidazol-2-yl)thio]-4 [(methylsulfonyl) amino]benzenesulfonamide,

5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-3-phenoxy-2(5H)-furanone,

N-[6-[(4-ethyl-2-thiazolyl)thio]-1,3-dihydro-1-oxo-5-isobenzofuranyl]methanesulfonamide,

3-[(2,4-dichlorophenyl)thio]-4-[(methylsulfonyl)amino] benzenesulfonamide,
1-fluoro-4-[2-[4-(methylsulfonyl)phenyl]cyclopenten-1-yl]benzene,
4-[5-(4-chlorophenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide,
3-[1-[4-(methylsulfonyl)phenyl]-4-(trifluoromethyl)-1H-imidazol-2-yl]pyridine,
4-[2-(3-pyridinyll)-4-(trifluoromethyl)-1H-imidazol-1-yl]benzenesulfonamide,
4-[5-(hydroxymethyl)-3-phenylisoxazol-4-yl]benzenesulfonamide,
4-[3-(4-chlorophenyl)-2,3-dihydro-2-oxo-4-oxazolyl]benzenesulfonamide,
4-[5-(difluoromethyl)-3-phenylisoxazol-4-yl]benzenesulfonamide,
[1,1':2',1"-terphenyl]-4-sulfonamide,
4-(methylsulfonyl)-1,1',2],1"-terphenyl,
4-(2-phenyl-3-pyridinyl)benzenesulfonamide,
N-(2,3-dihydro-1,1-dioxido-6-phenoxy-1,2-benzisothiazol-5-yl)methanesulfonamide,
N-[3-(formylamino)-4-oxo-6-phenoxy-4H-1-benzopyran-7-yl]methanesulfonamide,
6-[[5-(4-chlorobenzoyl)-1,4—dimethyl-1H-pyrrol-2-yl]methyl]-3(2H)-pyridazinone, and
N-(4-nitro-2-phenoxyphenyl)methanesulfonamide.

59. (Withdrawn) The pharmaceutical composition of claim 58 wherein the selective COX-2 inhibiting agent is rofecoxib.

60. (Original) The pharmaceutical composition of claim 58 wherein the selective COX-2 inhibiting agent is celecoxib.

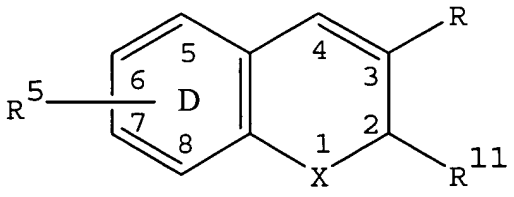
61. (Withdrawn) The pharmaceutical composition of claim 58 wherein the selective COX-2 inhibiting agent is valdecoxib.

62. (Withdrawn) The pharmaceutical composition of claim 58 wherein the selective COX-2 inhibiting agent is deracoxib.

63. (Withdrawn) The pharmaceutical composition of claim 58 wherein the selective COX-2 inhibiting agent is 4-(4-cyclohexyl-2-methyloxazol-5-yl)-2-fluorobenzenesulfonamide.

64. (Withdrawn) The pharmaceutical composition of claim 58 wherein the selective COX-2 inhibiting agent is etoricoxib.

65. (Withdrawn) The pharmaceutical composition of claim 50 wherein the selective COX-2 inhibiting agent is selected from compounds of Formula 2:



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or an isomer or pharmaceutically-acceptable salt or prodrug thereof, wherein

X is selected from the group consisting of O, S and NR^a;

R^a is alkyl;

R is selected from the group consisting of carboxyl, alkyl, aralkyl, aminocarbonyl, alkylsulfonylaminocarbonyl and alkoxycarbonyl;

R^{11} is selected from the group consisting of haloalkyl, alkyl, aralkyl, cycloalkyl and aryl, wherein aryl is optionally substituted with one or more radicals selected from the group consisting of alkylthio, nitro and alkylsulfonyl; and

R^5 is one or more radicals independently selected from the group consisting of hydrido, halo, alkyl, aralkyl, alkoxy, aryloxy, heteroaryloxy, aralkyloxy, heteroaralkyloxy, haloalkyl, haloalkoxy, alkylamino, arylamino, aralkylamino, heteroarylamino, heteroarylalkylamino, nitro, amino, aminosulfonyl, alkylaminosulfonyl, arylaminosulfonyl, heteroarylaminosulfonyl,

aralkylaminosulfonyl, heteroaralkylaminosulfonyl, heterocyclosulfonyl, alkylsulfonyl, optionally substituted aryl, optionally substituted heteroaryl, aralkylcarbonyl, heteroarylcarbonyl, arylcarbonyl, aminocarbonyl, and alkylcarbonyl, wherein R^5 together with ring D optionally forms a naphthyl radical.

66. (Withdrawn) The pharmaceutical composition of claim 65 wherein X is selected from the group consisting of O and S.

67. (Withdrawn) The pharmaceutical composition of claim 65 wherein R is selected from the group consisting of carboxyl, lower alkyl, lower aralkyl and lower alkoxycarbonyl.

68. (Withdrawn) The pharmaceutical composition of claim 67 wherein R is carboxyl.

69. (Withdrawn) The pharmaceutical composition of claim 65 wherein R^{11} is selected from the group consisting of lower haloalkyl, lower cycloalkyl and phenyl.

70. (Withdrawn) The pharmaceutical composition of claim 69 wherein R^{11} is lower haloalkyl.

71. (Withdrawn) The method of claim 70 wherein R^{11} is selected from the group consisting of fluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, difluoromethyl, and trifluoromethyl.

72. (Withdrawn) The pharmaceutical composition of claim 71 wherein R^{11} is selected from the group consisting of trifluoromethyl and pentafluorethyl.

73. (Withdrawn) The pharmaceutical composition of claim 65 wherein R^5 is one or more radicals independently selected from the group consisting of hydrido, halo, lower alkyl, lower alkoxy, lower haloalkyl, lower haloalkoxy, lower alkylamino, nitro, amino, aminosulfonyl, lower alkylaminosulfonyl, 5- or 6- membered heteroarylalkylaminosulfonyl, lower aralkylaminosulfonyl, 5- or 6- membered nitrogen containing heterocyclosulfonyl, lower alkylsulfonyl, optionally substituted phenyl, lower aralkylcarbonyl, and lower alkylcarbonyl.

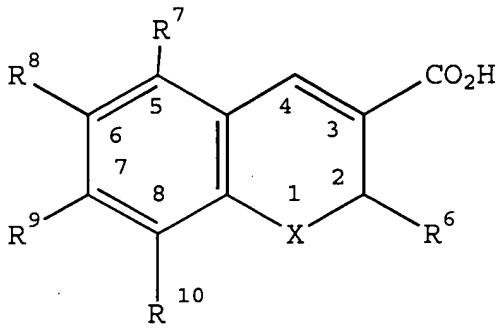
74. (Withdrawn) The pharmaceutical composition of claim 73 wherein R^5 is one or more radicals independently selected from the group consisting of hydrido, chloro, fluoro, bromo, iodo, methyl, ethyl, isopropyl, *tert*-butyl, butyl, isobutyl, pentyl, hexyl, methoxy, ethoxy, isopropyloxy, tertbutyloxy, trifluoromethyl, difluoromethyl, trifluoromethoxy, amino, N,N-dimethylamino, N,N-diethylamino, N-phenylmethylaminosulfonyl, N-phenylethylaminosulfonyl, N-(2-furylmethyl)aminosulfonyl, nitro, N,N-dimethylaminosulfonyl, aminosulfonyl, N-methylaminosulfonyl, N-ethylsulfonyl, 2,2-dimethylethylaminosulfonyl, N,N-dimethylaminosulfonyl, N-(2-methylpropyl)aminosulfonyl, N-morpholinosulfonyl, methylsulfonyl, benzylcarbonyl, 2,2-dimethylpropylcarbonyl, phenylacetyl and phenyl.

75. (Withdrawn) The pharmaceutical composition of claim 74 wherein R^5 is one or more radicals independently selected from the group consisting of hydrido, chloro, fluoro, bromo, iodo, methyl, ethyl, isopropyl, *tert*-butyl, methoxy, trifluoromethyl, trifluoromethoxy, N-phenylmethylaminosulfonyl, N-phenylethylaminosulfonyl, N-(2-furylmethyl)aminosulfonyl, N,N-dimethylaminosulfonyl, N-methylaminosulfonyl, N-(2,2-dimethylethyl)aminosulfonyl, dimethylaminosulfonyl, 2-methylpropylaminosulfonyl, N-morpholinosulfonyl, methylsulfonyl, benzylcarbonyl, and phenyl.

76. (Withdrawn) The pharmaceutical composition of claim 65 wherein the selective COX-2 inhibiting agent is selected from the group consisting of
6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
2-trifluoromethyl-3H-naphthopyran-3-carboxylic acid,
7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-bromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
5,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
7,8-dimethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid
6,8-bis(dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
7-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-8-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,8-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
2-trifluoromethyl-3H-naptho[2,1-b]pyran-3-carboxylic acid,
6-chloro-8-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-6-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-bromo-8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-bromo-6-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-bromo-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-bromo-5-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-8-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-bromo-8-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[[(phenylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[(dimethylamino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[(methylamino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[(4-morpholino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[(1,1-dimethylethyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[(2-methylpropyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-methylsulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-6-[[(phenylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-phenylacetyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,8-dibromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-5,6-dimethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,8-dichloro-(*S*)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-benzylsulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[[N-(2-furylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[[N-(2-phenylethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-iodo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
7-(1,1-dimethylethyl)-2-pentafluoroethyl-2H-1-benzopyran-3-carboxylic acid, and
6-chloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid.

77. (Withdrawn) The pharmaceutical composition of claim 47 wherein the selective COX-2 inhibiting agent is selected from compounds of Formula 3:



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or an isomer or pharmaceutically-acceptable salt or prodrug thereof, wherein

X is selected from the group consisting of O and S;

R^6 is lower haloalkyl;

R^7 is selected from the group consisting of hydrido and halo;

R^8 is selected from the group consisting of hydrido, halo, lower alkyl, lower haloalkoxy, lower alkoxy, lower aralkylcarbonyl, lower dialkylaminosulfonyl, lower alkylaminosulfonyl, lower aralkylaminosulfonyl, lower heteroaralkylaminosulfonyl, and 5- or 6- membered nitrogen containing heterocyclosulfonyl;

R^9 is selected from the group consisting of hydrido, lower alkyl, halo, lower alkoxy, and aryl; and

R^{10} is selected from the group consisting of hydrido, halo, lower alkyl, lower alkoxy, and aryl.

78. (Withdrawn) The pharmaceutical composition of claim 77 wherein R^6 is selected from the group consisting of trifluoromethyl and pentafluoroethyl.

79. (Withdrawn) The pharmaceutical composition of claim 77 wherein R^7 is selected from the group consisting of hydrido, chloro, and fluoro.

80. (Withdrawn) The pharmaceutical composition of claim 77 wherein R^8 is selected from the group consisting of hydrido, chloro, bromo, fluoro, iodo, methyl, tert-butyl, trifluoromethoxy, methoxy, benzylcarbonyl, dimethylaminosulfonyl,

isopropylaminosulfonyl, methylaminosulfonyl, benzylaminosulfonyl, phenylethylaminosulfonyl, methylpropylaminosulfonyl, methylsulfonyl, and morpholinosulfonyl.

81. (Withdrawn) The pharmaceutical composition of claim 77 wherein R^9 is selected from the group consisting of hydrido, methyl, ethyl, isopropyl, tert-butyl, chloro, methoxy, diethylamino, and phenyl.

82. (Withdrawn) The pharmaceutical composition of claim 77 wherein R^{10} is selected from the group consisting of hydrido, chloro, bromo, fluoro, methyl, ethyl, tert-butyl, methoxy, and phenyl.

83. (Withdrawn) The pharmaceutical composition of claim 77 wherein the selective COX-2 inhibiting agent is selected from the group consisting of
6-Chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-Chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-Chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-Chloro-7-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-Trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-Trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-Formyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-(Difluoromethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,8-Dichloro-7-methyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,8-Dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6,8-Dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-Chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
(S)-6-chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
6,8-Dichloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
7-(1,1-Dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6,7-Dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
5,6-Dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
2,6-Bis(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
5,6,7-Trichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,7,8-Trichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-Iodo-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
6-Bromo-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
6-Chloro-7-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid, and
6,8-Dichloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid.

84. (Withdrawn) The pharmaceutical composition of claim 83 wherein the selective COX-2 inhibiting agent is selected from the group consisting of
6-Chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-Chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-Chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-Chloro-7-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-Trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-Trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-Formyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-(Difluoromethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,8-Dichloro-7-methyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,8-Dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6,8-Dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-Chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
(S)-6-chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid, and
6,8-Dichloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid.

85. (Withdrawn) The pharmaceutical composition of claim 47 wherein the selective COX-2 inhibiting agent is selected from compounds that correspond in structure, and pharmaceutically acceptable salts thereof, of the group consisting of:

N-(2,3-dihydro-1,1-dioxido-6-phenoxy-1,2-benzisothiazol-5-yl)methanesulfonamide,

6-[[5-(4-chlorobenzoyl)-1,4—dimethyl-1H-pyrrol-2-yl]methyl]-3(2H)-pyridazinone,

N-(4-nitro-2-phenoxyphenyl)methanesulfonamide,

3-(3,4-difluorophenoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-2(5H)-furanone,

N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,

N-[2-(cyclohexyloxy)-4-nitrophenyl]methanesulfonamide,

N-[6-(2,4-difluorophenoxy)-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,

3-(4-chlorophenoxy)-4-[(methylsulfonyl)amino]benzenesulfonamide,

3-(4-fluorophenoxy)-4-[(methylsulfonyl)amino]benzenesulfonamide,

3-[(1-methyl-1H-imidazol-2-yl)thio]-4 [(methylsulfonyl) amino]benzenesulfonamide,

5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-3-phenoxy-2(5H)-furanone,

N-[6-[(4-ethyl-2-thiazolyl)thio]-1,3-dihydro-1-oxo-5-isobenzofuranyl]methanesulfonamide,

3-[(2,4-dichlorophenyl)thio]-4-[(methylsulfonyl)amino]benzenesulfonamide,

N-(2,3-dihydro-1,1-dioxido-6-phenoxy-1,2-benzisothiazol-5-yl)methanesulfonamide, and

N-[3-(formylamino)-4-oxo-6-phenoxy-4H-1-benzopyran-7-yl]methanesulfonamide.

86. (Original) The pharmaceutical composition of claim 47 wherein the neoplasia disorder is selected from the group consisting of a lung, a breast, a skin, a stomach, an intestine, an esophagus, a bladder, a head, a neck, a brain, a cervical, and an ovary neoplasia disorder.

87. (Original) The pharmaceutical composition of claim 47 wherein the neoplasia disorder is selected from the group consisting of acral lentiginous melanoma, an actinic keratosis, adenocarcinoma, adenoid cycstic carcinoma, an adenoma,

adenosarcoma, adenosquamous carcinoma, an astrocytic tumor, bartholin gland carcinoma, basal cell carcinoma, a bronchial gland carcinoma, capillary carcinoma, a carcinoid, carcinoma, carcinosarcoma, cavernous carcinoma, cholangiocarcinoma, chondosarcoma, choriod plexus papilloma, choriod plexus carcinoma, clear cell carcinoma, cystadenoma, endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, ependymal carcinoma, epitheloid carcinoma, Ewing's sarcoma, fibrolamellar, focal nodular hyperplasia, gastrinoma, a germ cell tumor, glioblastoma, glucagonoma, hemangiblastoma, hemangioendothelioma, a hemangioma, hepatic adenoma, hepatic adenomatosis, hepatocellular carcinoma, insulinoma, intaepithelial neoplasia, interepithelial squamous cell neoplasia, invasive squamous cell carcinoma, large cell carcinoma, leiomyosarcoma, a lentigo maligna melanoma, malignant melanoma, a malignant mesothelial tumor, medulloblastoma, medulloepithelioma, melanoma, meningeal, mesothelial, metastatic carcinoma, mucoepidermoid carcinoma, neuroblastoma, neuroepithelial adenocarcinoma nodular melanoma, oat cell carcinoma, oligodendroglial, osteosarcoma, pancreatic polypeptide, papillary serous adenocarcinoma, pineal cell, a pituitary tumor, plasmacytoma, pseudosarcoma, pulmonary blastoma, renal cell carcinoma, retinoblastoma, rhabdomyosarcoma, sarcoma, serous carcinoma, small cell carcinoma, a soft tissue carcinoma, somatostatin-secreting tumor, squamous carcinoma, squamous cell carcinoma, submesothelial, superficial spreading melanoma, undifferentiated carcinoma, uveal melanoma, verrucous carcinoma, vipoma, a well differentiated carcinoma, and Wilm's tumor.

88. (Original) The pharmaceutical composition of claim 47 wherein the composition is provided as a separate component of a kit.

89. (Original) The pharmaceutical composition of claim 47 wherein the composition is administered orally, rectally, topically, bucally, or parenterally.

90. (Original) The pharmaceutical composition of claim 47 wherein the composition is a tablet, capsule, cachet, lozenge, dispensable powder, granule, solution, suspension, emulsion or liquid.

91. (Original) The pharmaceutical composition of claim 47 wherein the selective COX-2 inhibiting agent is present in an amount from about 0.1 mg to about 10,000 mg.

92. (Original) The pharmaceutical composition of claim 47 wherein the DNA topoisomerase I inhibiting agent is present in an amount from about 0.001 mg to about 10,000 mg.

93. to 97. (Canceled)

98. (Withdrawn) The use of claim 97 wherein A is substituted with one or more radicals selected from the group consisting of alkyl, halo, oxo, hydroxy and alkoxy.

99. to 104. (Canceled).

105. (Withdrawn) The use of claim 104 wherein the selective COX-2 inhibiting agent is rofecoxib.

106. (Canceled)

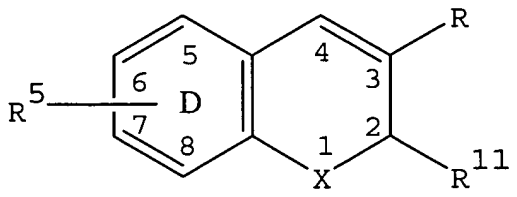
107. (Withdrawn) The use of claim 104 wherein the selective COX-2 inhibiting agent is valdecoxib.

108. (Withdrawn) The use of claim 104 wherein the selective COX-2 inhibiting agent is deracoxib.

109. (Withdrawn) The use of claim 104 wherein the selective COX-2 inhibiting agent is 4-(4-cyclohexyl-2-methyloxazol-5-yl)-2-fluorobenzenesulfonamide.

110. (Withdrawn) The use of claim 104 wherein the selective COX-2 inhibiting agent is etoricoxib.

111. (Withdrawn) The use of claim 93 wherein the selective COX-2 inhibiting agent is selected from compounds of Formula 2:



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or an isomer or pharmaceutically-acceptable salt or prodrug thereof, wherein

X is selected from the group consisting of O, S and NR^a;

R^a is alkyl;

R is selected from the group consisting of carboxyl, alkyl, aralkyl, aminocarbonyl, alkylsulfonylaminocarbonyl and alkoxycarbonyl;

R^{11} is selected from the group consisting of haloalkyl, alkyl, aralkyl, cycloalkyl and aryl, wherein aryl is optionally substituted with one or more radicals selected from the group consisting of alkylthio, nitro and alkylsulfonyl; and

R^5 is one or more radicals independently selected from the group consisting of hydrido, halo, alkyl, aralkyl, alkoxy, aryloxy, heteroaryloxy, aralkyloxy, heteroaralkyloxy, haloalkyl, haloalkoxy, alkylamino, arylamino, aralkylamino, heteroarylamino, heteroarylalkylamino, nitro, amino, aminosulfonyl, alkylaminosulfonyl, arylaminosulfonyl, heteroarylaminosulfonyl, aralkylaminosulfonyl, heteroaralkylaminosulfonyl, heterocyclosulfonyl,

alkylsulfonyl, optionally substituted aryl, optionally substituted heteroaryl, aralkylcarbonyl, heteroarylcarbonyl, arylcarbonyl, aminocarbonyl, and alkylcarbonyl, wherein R^5 together with ring D optionally forms a naphthyl radical.

112. (Withdrawn) The use of claim 111 wherein X is selected from the group consisting of O and S.

113. (Withdrawn) The use of claim 111 wherein R is selected from the group consisting of carboxyl, lower alkyl, lower aralkyl and lower alkoxycarbonyl.

114. (Withdrawn) The use of claim 113 wherein R is carboxyl.

115. (Withdrawn) The use of claim 111 wherein R^{11} is selected from the group consisting of lower haloalkyl, lower cycloalkyl and phenyl.

116. (Withdrawn) The use of claim 115 wherein R^{11} is lower haloalkyl.

117. (Withdrawn) The method of claim 115 wherein R^{11} is selected from the group consisting of fluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, difluoromethyl, and trifluoromethyl.

118. (Withdrawn) The use of claim 117 wherein R^{11} is selected from the group consisting of trifluoromethyl and pentafluorethyl.

119. (Withdrawn) The use of claim 111 wherein R^5 is one or more radicals independently selected from the group consisting of hydrido, halo, lower alkyl, lower alkoxy, lower haloalkyl, lower haloalkoxy, lower alkylamino, nitro, amino, aminosulfonyl, lower alkylaminosulfonyl, 5- or 6- membered heteroarylalkylaminosulfonyl, lower aralkylaminosulfonyl, 5- or 6- membered

nitrogen containing heterocyclosulfonyl, lower alkylsulfonyl, optionally substituted phenyl, lower aralkylcarbonyl, and lower alkylcarbonyl.

120. (Withdrawn) The use of claim 119 wherein R^5 is one or more radicals independently selected from the group consisting of hydrido, chloro, fluoro, bromo, iodo, methyl, ethyl, isopropyl, *tert*-butyl, butyl, isobutyl, pentyl, hexyl, methoxy, ethoxy, isopropyloxy, tertbutyloxy, trifluoromethyl, difluoromethyl, trifluoromethoxy, amino, N,N-dimethylamino, N,N-diethylamino, N-phenylmethylaminosulfonyl, N-phenylethylaminosulfonyl, N-(2-furylmethyl)aminosulfonyl, nitro, N,N-dimethylaminosulfonyl, aminosulfonyl, N-methylaminosulfonyl, N-ethylsulfonyl, 2,2-dimethylethylaminosulfonyl, N,N-dimethylaminosulfonyl, N-(2-methylpropyl)aminosulfonyl, N-morpholinosulfonyl, methylsulfonyl, benzylcarbonyl, 2,2-dimethylpropylcarbonyl, phenylacetyl and phenyl.

121. (Withdrawn) The use of claim 120 wherein R^5 is one or more radicals independently selected from the group consisting of hydrido, chloro, fluoro, bromo, iodo, methyl, ethyl, isopropyl, *tert*-butyl, methoxy, trifluoromethyl, trifluoromethoxy, N-phenylmethylaminosulfonyl, N-phenylethylaminosulfonyl, N-(2-furylmethyl)aminosulfonyl, N,N-dimethylaminosulfonyl, N-methylaminosulfonyl, N-(2,2-dimethylethyl)aminosulfonyl, dimethylaminosulfonyl, 2-methylpropylaminosulfonyl, N-morpholinosulfonyl, methylsulfonyl, benzylcarbonyl, and phenyl.

122. (Withdrawn) The use of claim 111 wherein the selective COX-2 inhibiting agent is selected from the group consisting of
6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

2-trifluoromethyl-3H-naphthopyran-3-carboxylic acid,

7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-bromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

5,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

8-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

7,8-dimethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid

6,8-bis(dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

7-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-chloro-7-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-chloro-8-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-chloro-7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6,8-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

2-trifluoromethyl-3H-naptho[2,1-b]pyran-3-carboxylic acid,

6-chloro-8-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

8-chloro-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

8-chloro-6-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-bromo-8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

8-bromo-6-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

8-bromo-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

8-bromo-5-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-chloro-8-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-bromo-8-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-[[(phenylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-[(dimethylamino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-[(methylamino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-[(4-morpholino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-[(1,1-dimethylethyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-

carboxylic acid,

6-[(2-methylpropyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-methylsulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

8-chloro-6-[[(phenylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-phenylacetyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6,8-dibromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

8-chloro-5,6-dimethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6,8-dichloro-(*S*)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-benzylsulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-[[N-(2-furylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

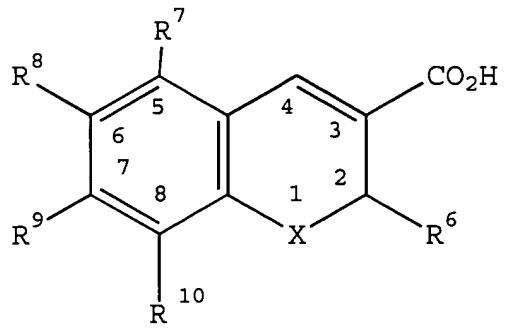
6-[[N-(2-phenylethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-iodo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

7-(1,1-dimethylethyl)-2-pentafluoroethyl-2H-1-benzopyran-3-carboxylic acid, and

6-chloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid.

123. (Withdrawn) The use of claim 93 wherein the selective COX-2 inhibiting agent is selected from compounds of Formula 3:



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or an isomer or pharmaceutically-acceptable salt or prodrug thereof,

wherein

X is selected from the group consisting of O and S;

R^6 is lower haloalkyl;

R^7 is selected from the group consisting of hydrido and halo;

R^8 is selected from the group consisting of hydrido, halo, lower alkyl, lower haloalkoxy, lower alkoxy, lower aralkylcarbonyl, lower dialkylaminosulfonyl, lower alkylaminosulfonyl, lower aralkylaminosulfonyl, lower heteroaralkylaminosulfonyl, and 5- or 6- membered nitrogen containing heterocyclosulfonyl;

R^9 is selected from the group consisting of hydrido, lower alkyl, halo, lower alkoxy, and aryl; and

R^{10} is selected from the group consisting of hydrido, halo, lower alkyl, lower alkoxy, and aryl.

124. (Withdrawn) The use of claim 123 wherein R^6 is selected from the group consisting of trifluoromethyl and pentafluoroethyl.

125. (Withdrawn) The use of claim 123 wherein R^7 is selected from the group consisting of hydrido, chloro, and fluoro.

126. (Withdrawn) The use of claim 123 wherein R^8 is selected from the group consisting of hydrido, chloro, bromo, fluoro, iodo, methyl, tert-butyl, trifluoromethoxy, methoxy, benzylcarbonyl, dimethylaminosulfonyl, isopropylaminosulfonyl, methylaminosulfonyl, benzylaminosulfonyl, phenylethylaminosulfonyl, methylpropylaminosulfonyl, methylsulfonyl, and morpholinosulfonyl.

127. (Withdrawn) The use of claim 123 wherein R^9 is selected from the group consisting of hydrido, methyl, ethyl, isopropyl, tert-butyl, chloro, methoxy, diethylamino, and phenyl.

128. (Withdrawn) The use of claim 123 wherein R^{10} is selected from the group consisting of hydrido, chloro, bromo, fluoro, methyl, ethyl, tert-butyl, methoxy, and phenyl.

129. (Withdrawn) The use of claim 123 wherein the selective COX-2 inhibiting agent is selected from the group consisting of
6-Chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-Chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-Chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-Chloro-7-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-Trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-Trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-Formyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-(Difluoromethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,8-Dichloro-7-methyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,8-Dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6,8-Dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-Chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
(S)-6-chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
6,8-Dichloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
7-(1,1-Dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,7-Dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
5,6-Dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
2,6-Bis(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
5,6,7-Trichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,7,8-Trichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-Iodo-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
6-Bromo-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
6-Chloro-7-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid, and
6,8-Dichloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid.

130. (Withdrawn) The use of claim 129 wherein the selective COX-2 inhibiting agent is selected from the group consisting of
6-Chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-Chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-Chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-Chloro-7-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-Trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-Trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-Formyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-(Difluoromethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,8-Dichloro-7-methyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,8-Dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6,8-Dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-Chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
(S)-6-chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid, and
6,8-Dichloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid.

131. (Withdrawn) The use of claim 93 wherein the selective COX-2 inhibiting agent is selected from compounds that correspond in structure, and pharmaceutically acceptable salts thereof, of the group consisting of:
N-(2,3-dihydro-1,1-dioxido-6-phenoxy-1,2-benzisothiazol-5-yl)methanesulfonamide,
6-[[5-(4-chlorobenzoyl)-1,4—dimethyl-1H-pyrrol-2-yl]methyl]-3(2H)-pyridazinone,
N-(4-nitro-2-phenoxyphenyl)methanesulfonamide,
3-(3,4-difluorophenoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-2(5H)-furanone,
N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,
N-[2-(cyclohexyloxy)-4-nitrophenyl]methanesulfonamide,

N-[6-(2,4-difluorophenoxy)-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,

3-(4-chlorophenoxy)-4-[(methylsulfonyl)amino]benzenesulfonamide,

3-(4-fluorophenoxy)-4-[(methylsulfonyl)amino]benzenesulfonamide,

3-[(1-methyl-1H-imidazol-2-yl)thio]-4 [(methylsulfonyl) amino]benzenesulfonamide,

5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-3-phenoxy-2(5H)-furanone,

N-[6-[(4-ethyl-2-thiazolyl)thio]-1,3-dihydro-1-oxo-5-isobenzofuranyl]methanesulfonamide,

3-[(2,4-dichlorophenyl)thio]-4-[(methylsulfonyl)amino]benzenesulfonamide,

N-(2,3-dihydro-1,1-dioxido-6-phenoxy-1,2-benzisothiazol-5-yl)methanesulfonamide, and

N-[3-(formylamino)-4-oxo-6-phenoxy-4H-1-benzopyran-7-yl]methanesulfonamide.

132. to 181. (Canceled).